



Review

Sulfur fumigation, a better or worse choice in preservation of Traditional Chinese Medicine?

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ABSTRACT

Sulfur fumigation (SF) in Traditional Chinese Medicine (TCM) is a highly efficient and important traditional preservation method in China. This method has generated a great deal of concern and has been disputed in the last few years because of its uncertain safety. SF can alter the quality of TCMs by damaging the bioactive compounds, changing chemical profiles, and generating detrimental exogenous materials. However, SF is still widely used in the herbal medicinal industry because of its various benefits, such as its pesticidal and anti-bacterial effects, easy operation, and low-cost. This review contains the current situation, chemical mechanism and reactions during SF, the pharmacological and pharmacokinetic research, and the influence of quality caused by SF. In addition, a quantification-operation sulfur fumigation device (QOSFD), which can maintain the quality of TCMs by controlling the SF processing parameters, has been designed and introduced. The key technologies of this device involve controlling the O_2 content and the temperature of SO_2 as well as the quantification of sulfur in SF. This device can reduce the possibility of reaction between bioactive compounds and sulfur/sulfurous acid, as well as control the limitation of SO_2 residues. The QOSFD is regarded as a promising preservation technique in the field of TCM, medicinal materials, agriculture, and fruit industry.

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Abbreviations: TCM, Traditional Chinese Medicine; SF, sulfur fumigation; SF-TCMs, sulfur fumigated TCMs; non-SF-TCMs, non-sulfur fumigated TCMs; PPRC, Pharmacopoeia of People's Republic of China; SFDA, State Food and Drug Administration; SPC, State Pharmacopoeia Committee; QOSFD, quantification-operation sulfur fumigation device.

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Introduction

Sulfur fumigation (SF) is an important method in preserving Traditional Chinese Medicines (TCMs). Given that most TCM herbs are derived from plant tissues and animal organs that contain large amount of water and nutrients, several TCMs undergo difficulties (insects, fungus, microbe, and moistures) in preservation.

Therefore, post-harvesting and preservation are necessary in TCM. The earliest record on preservation in TCM was from the “Sheng Nong’s Herbal Classic (Shen Nong Ben Cao Jing)” (Anonymous 1955), which has a history of almost 5000 years. Preservations in TCM were constantly optimized and developed in history. At present, SF is widely applied in TCM processing factories in China, such as during the post-harvest processing of *Dioscoreae rhizoma* (shan yao), *Angelicae dahuricae radix* (bai zhi), and *Chrysanthemi flos* (ju hua). However, sulfur-fumigated TCMs (SF-TCMs) have recently emerged as a controversial topic because of the following reasons: (1) consumer complaints because of the side effect of sulfur itself; (2) increasing concern on the residues in SO₂ and detrimental heavy metals in TCMs; and (3) high amounts of residues in SO₂ and heavy metals and a decrease in the bioactive compounds revealed by a chemical analysis. In 2004, the State Food and Drug Administration (SFDA) of China officially assigned SF-TCMs as inferior quality TCMs. In the academe, several pharmacological experiments and chemical analysis have been performed in this field. Moreover, the SFDA of China established several regulations since 2011 (State Food and Drug Administration 2012). This review will focus on the current application of SF in TCMs in China, analyze the influence of SF on the safety and quality of TCMs, discusses whether SF should be still be applied, and introduce the quantification-operation sulfur fumigation device (QOSFD).

History and current situation of SF in TCMs

In 1900, SF processing was first applied in the processing and storage of *D. rhizoma* (guang shanyao) in Wenzhou (Anonymous 1991). Considering its efficiency, lower cost, and feasible operation, SF was soon accepted by manufacturers. SF was first recorded on the preservation of *Achyranthis bidentatae radix* (niu xi) in the Pharmacopoeia of the People’s Republic of China (PPRC) (1963 version) (State Pharmacopoeia Committee, 1963). Subsequently, four TCMs were added in the 1977 version of PPRC (SPC, 1977), including *Typhonii rhizoma* (bai fu zi), *D. rhizoma* (shan yao), *Puerariae radix* (ge gen), and *Lonicerae flos* (jin yin hua). This inclusion persisted in the 1985 and 1990 versions of PPRC. The 1995 version of PPRC (SPC 1995) recorded six herbs that can be processed by SF, including *D. rhizoma* (shan yao), *A. bidentatae radix* (niu xi), *Aconiti lateralis preparata radix* (fu zi), *T. rhizoma* (bai fu zi), and *L. Flos* (jin yin hua). In the 2000 version of PPRC (SPC 2000), the permitted SF-TCMs were reduced to three, including *Fritilariae hupehensis bulbus* (hubei bei mu), *P. radix* (ge gen), and *D. rhizoma* (shan yao). Other herbs were no longer permitted with SF processing in the 2005 version of PPRC (SPC 2005). Since 2005, PPRC recorded the detailed determination method of SO₂ residues in TCMs. Given the insufficiency of the theoretical data in this field, the nationally regulated SO₂ content in most SF-TCMs has not been promulgated yet. In 2011, the SFDA of China regulated the quantity of SO₂ in TCMs. TCMs are divided into two categories. The first category, which limits the SO₂ to not more than 400 mg/kg, includes 11 herbs, namely, *D. rhizoma* (shan yao), *A. bidentatae radix* (niu xi), *P. Thomsonii radix* (fen ge), *Kansui radix* (gan sui), *Gastrodiae rhizome* (tian ma), *Asparagi radix* (tian dong), *Trichosanthis radix* (tian hua fen), *Bletillae rhizome* (bai ji), *Paoniae radix alba* (bai shao), *Atractylodis macrocephalae rhizome* (bai zhu), and *Codonopsis radix* (dang shen). The second category, with a quantity limitation not exceeding 150 mg/kg, includes all other TCMs, except for the species in the first category (State Food and Drug Administration 2012).

Although PPRC deleted the SF method in processing TCMs in 2005, this process is still presently applied in commercial TCMs. The following types of TCMs urgently require SF processing: (1) The radix and rhizoma that contain abundant starch and polysaccharide, such as *D. rhizome* (shan yao), *P. Thomsonii radix* (fen

ge), *T. radix* (tian hua fen), *C. radix* (dang shen), *A. dahuricae radix* (bai zhi), *P. radix alba* (bai shao), *A. macrocephalae rhizome* (bai zhu), *A. sinensis radix* (dang gui), *Chuanxiong rhizoma* (chuan xiong), *Changii radix* (ming dang shen), *Adenophorae radix* (nan sha shen), and *Alismatis Rhizome* (ze xie); (2) TCMs from the organs of animals that contain certain amount of proteins, fat, and amino acid, such as the Hippocampus (hai ma), Syngnathus (hai long), *Eupolyphaga steleophaga* (tu bie chong), and Hirudo (shui zhi); and (3) medicines with appearance, color, and odor that can be easily altered by the surroundings, such as *L. japonicae flos* (jin yin hua), and *C. flos* (ju hua) (Duan et al. 2011). Considering the appearance of medicinal materials from animals that can be affected by SF, manufacturers seldom use this process in animal medicines. Although this method is originally applied in several herbs, the producers in China use SF in almost all species because of its efficiency and convenience. According to a market survey, eight TCMs exhibited the most serious challenges with SF, namely, *F. hupehensis bulbus* (hubei bei mu), *A. sinensis radix* (dang gui), *Gastrodiae rhizome* (tian ma), *D. rhizoma* (Shan Yao), *P. radix alba* (bai shao), *C. flos* (ju hua), *C. radix* (dang shen), and *Lycii fructus* (gou qi zi). The manufacturers prefer SF in producing decoction pieces because of the following reasons: (1) SF can produce a desirable appearance for TCMs; (2) SF-TCMs contain more water (20–30%) compared with sun-dried TCMs (15%), resulting in SF-TCMs with higher weight (Weng 2011). These factors lead to the lower price of non-SF-TCMs in the market. Several fruits and crops are reportedly treated similarly to keep the desirable appearance in the market, such as litchi, banana, corn, and bean (Cantin et al. 2010, 2011; Lorenzini et al. 1990). Post-harvest SF was a conventional method used by cultivators for fruits and crops, although it is not a statutory method. Aside from China, this technique is also used in other countries, including several developed countries (e.g., USA and Italy) and developing countries (e.g., Thailand and Vietnam) (Lorenzini et al. 1990). Given the increasing restriction on SO₂ residues and negative influence of SF to the quality of products, researchers in the fields of food and agriculture attempt to improve post-harvesting methods and alternatives. Therefore, optimized preservation should be explored in the field of TCM.

Basic information on SF in TCMs

Procedures of SF

Low-cost SF method is easy to operate, and the device is simple and crude. The amount of sulfur, fumigation time, fumigation frequency, and exhaustion time usually depend on the amount of TCM materials. First, a chamber with a side window and a net-like spacer plate in the space are needed. During operation, TCMs should be equidistantly positioned on the netlike spacer plate. Second, certain amounts of sulfur (normally, 1 g sulfur per 20 g TCM materials) are placed in an enameled ware positioned at the bottom of this chamber. Third, the window of chamber should be closed after the sulfur is ignited. The chamber should be obturated when an obvious blue-flame is generated. Fourth, after a certain amount of time (this period ranges from 2 h to 2 d depending on the amount of materials), the chamber could be opened for gas emission (exhaustion time ranges from 2 h to 2 d). These parameters in SF are rough during operations. Most manufacturers operate SF depending on the appearance of the TCMs. This method influences the quality of TCMs, as well as pollutes the environment with the exhaust gas. SF can enhance the appearance of medicinal materials. Even decayed medicinal materials can present a fresh appearance after SF. SF-TCMs have sour and irritant taste, producing an undesired taste when the SO₂ content exceeds 0.05% (Brannen 1985).

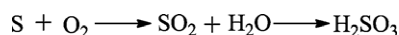


Fig. 1. The formula of the basic reaction of SF.

Chemical mechanism of the function of SF

Sulfur is a yellow powder or sheet-shape and easily ignites. During sulfur combustion, SO_2 is produced by the combination of sulfur and oxygen, and sulfurous acid is generated by the combination of SO_2 and water molecule (Fig. 1). SO_2 can kill several microbes, fungus, and insects. Sulfurous acid is reducible and can serve for bleaching and anticorrosion. The whole process of SF eliminates the moistures in the materials of TCMs.

SF in processing TCMs has efficient anti-insect, antimicrobial, and anti-fungus effects. Gaseous SO_2 can directly kill larva and insects, which damages the medicines. SO_2 inhibits the bioactivity of almost all kinds of fungus. Second, sulfurous acid is always regarded as acid aseptic because it can consume the oxygen in the TCM issues and inhibit the bioactivity of necessary enzymes in microorganisms (Duan et al. 2011).

SF can bleach color materials and maintain a desirable appearance of TCMs. The change in the color in TCMs comes from enzymatic and non-enzymatic browning. On one side, enzymatic browning is relative to the activity of oxidase. In SF, sulfurous acid as a reducible compound, strongly inhibits the activity of oxidase, thereby effectively inhibiting enzymatic browning. However, non-enzymatic browning reaction (Millard Reaction) that occurs between amino acid and glucose is another primary factor in the changing of color in TCMs. Additional reaction can happen with the existence of sulfurous acid and glucose. The products of the additional reaction cannot be ketonized, thereby inhibiting the condensation reaction between the amino acid and carbonyl groups in the compounds (Duan et al. 2011). TCM herbs can maintain a desirable appearance because of bleaching.

Benefits and adverse effects of SF in the TCMs

TCM quality depends on their preservation process. Storage efficiency is the most important characteristic of SF. TCMs containing certain water and resource of carbon, as well as nitrogen, easily lead to decay and release even the more toxic aflatoxin in storage when they were not be dried definitely. Studies on the efficacy of different storage methods show that SF has the highest efficiency (Zhang et al. 2004). SF is efficient, easy to operate, and has low operational cost. In addition, this process can maintain the desirable appearance of TCMs, which can demand a higher TCM price in the market. Hence, manufacturers are inclined to use SF.

SF generates several risks, chemically and pharmacologically. First, this process can damage bioactive compounds and chemical profiles in TCMs, which can influence the quality of the original TCMs. Second, SF can produce a number of unknown compounds that have been relatively unexplored. These unknown compounds may pose pharmacological risk. Third, the most serious effects of SF-TCMs are the SO_2 residuals and excessive amount of heavy metals. Almost all TCMs roughly processed by SF present a high level of SO_2 and heavy metals. Finally, in terms of the economy and market, SF can easily alter the appearance and weight of TCMs as a method of counterfeiting (Weng 2011). Therefore, risks definitely exist in SF-TCMs.

Influence of SF in the quality of TCMs

TCM herbs contain complex compounds that react with sulfur or sulfurous acid during fumigation. Volatile oils, lactones, glycosides, phenolic acid, protein, and saccharides can also be transformed in this process. The content of several compounds can be reduced

because of the unclear mechanism in chemical reactions, which drastically influence the quality of TCMs. New compounds may be created in this process. The combination of constituents and chemical profiles of original TCM herbs can be changed dramatically by these two ways. In addition, SO_2 , trace elements (including detrimental heavy metals), and dust may be added into the TCMs. All these factors seriously influence the quality of the TCMs.

Chemical reaction between sulfur/sulfurous acid and components in TCMs

First, the lactones can engender the complex reaction as oxidation and enzymolysis during SF. In this process, lactone ring can be opened and oxidized in the acid condition. This condition leads to the oxidation of the olefinic bond and the reduction of lactones. The typical reaction is the reaction of coumarin and ligustilide (Figs. 2 and 3). With SF, the content of coumarins (such as imperatorin, isoimperatorin, and oxypeucedanin) decreased dramatically in *A. Dahuricae radix* (bai zhi). New peaks were produced in SF-*A. D. radix* (bai zhi), whereas other components disappeared (Zhang et al. 2005; Wang et al. 2009; Fan et al. 2011). SF is regarded as an unacceptable approach because of the serious degradation of bioactive compounds in processed TCMs.

Glycosides can also be transformed in SF. Complex reactions involving bioactive compounds and enzymes are found in this process. *Ginseng radix et rhizoma* (ren shen) contains ginsenoside and hydrolase that can be hydrolyzed into sapogenin, and sulfur can damage the hydrolase, thereby preventing the hydrolysis of ginsenoside. However, ginsenoside can also be hydrolyzed by sulfurous acid (Li et al. 1995). When white ginseng (bai shen) is sulfur-fumigated, its original ginsenosides (bai shen) are transformed into various sulfur artifacts, such as ginsenoside Rb1 sulfate (Li et al. 2012). Previous studies on *P. radix Alba* (bai shao) revealed the conversion of the main component, paeoniflorin, into its sulfonate derivative, paeoniflorin sulfonate (Wang et al. 2007a; Hayes et al. 2005). Six monoterpene glycoside sulfonate derivatives were detected in commercial *P. radix Alba* (bai shao), suggesting that the main monoterpene glycosides, such as galloylpaeoniflorin, mudanpioside E, oxypaeoniflorin, and benzoylpaeoniflorin, can also be easily converted into their sulfonate derivatives (Li et al. 2009; Cheng et al. 2010b). Other previous studies also reported on the decreasing bioactive compounds with unclear mechanism. The content of gastrodin and lobetyolin decreased in SF-*G. rhizoma* (tian ma) (Wu and Zhu 2010) and *C. radix* (dang shen) (Wang et al. 2006), respectively.

Volatile compounds in TCM herbs can easily be transformed in this process. Low-boiling-point volatile compounds, especially monoterpene and sesquiterpenes, can be involved in the chemical reactions, such as sulfur-unsaturated alkene and sulfur-aromatic hydrocarbon reactions (Duan et al. 2011). These reactions usually occur in *A. sinensis radix* (dang gui), *C. rhizoma* (chuan xiong), *A. macrocephalae rhizoma* (bai zhu). The possible reaction process is presented in Fig. 4 (Duan et al. 2011). A considerable difference was found in the compositions of the two samples, *C. flos* and SF-*C. flos*, which are mainly in terpene and sesquiterpene. The yield of the volatile compounds in the wind-drying *C. flos* was 3.50%, whereas the yield in SF-*C. flos* was 4.22%. The compositions of SF-*C. flos* were significantly altered after SF, including the reduction of certain bio-constituents (such as eucalyptol, umbellulone, carvacrol, caryophyllene oxide, and ledol, which have antimicrobial and antiphlogosis effects) and the addition of other bio-constituents (such as α -pinene, β -pinene, camphene, camphor, borneol, α -terpineol, verbenol acetate, bomy acetate, *cis*-caryophyllene, and longipinocarvone). The complex additions and reductions may have led to the higher yield of volatile compounds in SF-*C. flos* or SF enhances the extraction efficiency of volatile compounds in

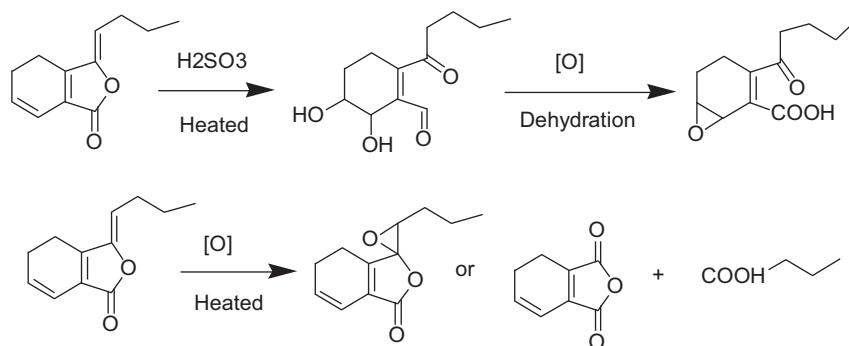


Fig. 2. The possible reaction of ligustilide in the process of SF.

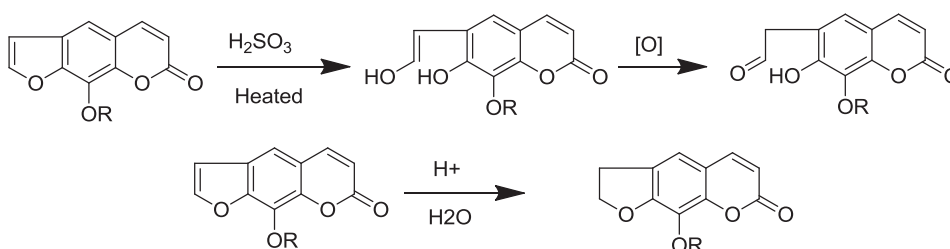


Fig. 3. The possible reaction of coumarin in the process of SF.

TCMs. The possible mechanisms of these complex reactions were analyzed according to the characteristics of the structures and by changing of the contents of these compounds in this experiment (Figs. 5 and 6) (Wang et al. 2007b; Demetzos et al. 1997). However, limited research has been performed on these new additions in the volatile compounds. Similarly, the research of *A. stellati fructus* (ba jiao hui xiang), the extraction ratio of the essential oil was 7.0% in non-SF-*A. stellati fructus* (ba jiao hui xiang), whereas the ratio increased to 10.8% in SF-*A. stellati fructus* (ba jiao hui xiang) (Liang et al. 2010). This condition implies the high yield of essential oil in SF-TCMs. The combination and contents of these compounds in these two samples also have significant differences. The SF-*A. stellati fructus* (ba jiao hui xiang) contain more types of essential oils possibly because of the degradation of the original essential oils. However, the main compound, trans-anethole in SF-*A. stellati fructus* (ba jiao hui xiang) decreased.

Phenolic acid, flavone, and alkaloids can also be changed during SF. Although most compounds decreased in SF-TCMs, certain compounds also increased. The content of chlorogenic acid in SF-*C. flos*

was higher than that treated by the natural drying method (Wang et al. 2007a,b). The content of chlorogenic acid can increase with an increase in the dosage of sulfur and number of SF treatments in SF-*C. flos*. This phenomenon is associated with the existence of polyphenol oxidase (PPO) in *C. flos*. Hydrosulfite produced by SF, such as NaHSO₃, can decrease the intensity of the enzymatic reaction of PPO and delay the time of reaction. In addition, NaHSO₃, as a reducible compound, can turn quinone, a phenol oxidation product, into phenol, thereby preventing the oxidation of chlorogenic acid and maintaining the chlorogenic acid in *C. flos*. However, quercetin, luteolin, and general flavone in SF-*C. flos* decreased (Zhao et al. 2010). Ferulic acid decreased in SF-*A. sinensis* (dang gui). The increased dosage, fumigation time, and fumigation frequency will aggravate this phenomenon (Li et al. 2011; Zhang et al. 2011a). Given the complex reactions, phenolic acids can be increased or decreased during SF. According to the limit reports, alkaloids decreased after SF. The total alkaloids in *Pinelliae Rhizoma* (ban xia) dramatically decreased after SF (Tang et al. 2003; Zhou et al. 2010). SF can decrease the contents of allantoin, a type of alkaloid in *D. rhizoma* (shao yao), with the increasing fumigation (Zhao et al. 2009).

The large bio-molecule, such as protein and saccharides, can be involved in the Maillard reactions during SF. The Maillard reaction comprises a series of reactions between the amino compounds, usually the amino acids or proteins, and carbohydrates. The Maillard reaction can be influenced by temperature and pH value (Liu et al. 2009). Polysaccharide sulfate can be produced by the reaction of saccharides and sulfurous acid because of the Maillard reaction. According to previous reports, the general saccharides, phospholipids, and saponin in *L. bulbis* (bai he) decreased after SF (Li et al. 2006). However, the saccharide in *D. rhizoma* (shan yao) increased with 3 g/kg of sulfur in the fumigation, but dropped dramatically when the amount of sulfur reaches 6–10 g/kg in the fumigation (Cui and Xin 2007). In a previous study on *P. rhizoma* (ban xia), the amino acids increased after SF (Wan et al. 2009), but the mechanism behind this phenomenon has not been explored. Thus, fumigation temperature is controlled strictly according to the mechanism of the Maillard reaction. Most of the main bioactive compounds in

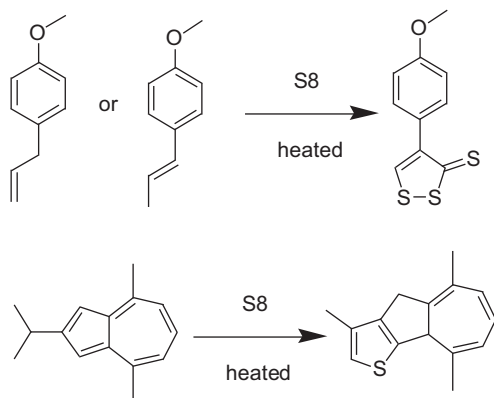


Fig. 4. The possible reaction of monoterpene, sesquiterpene in SF.

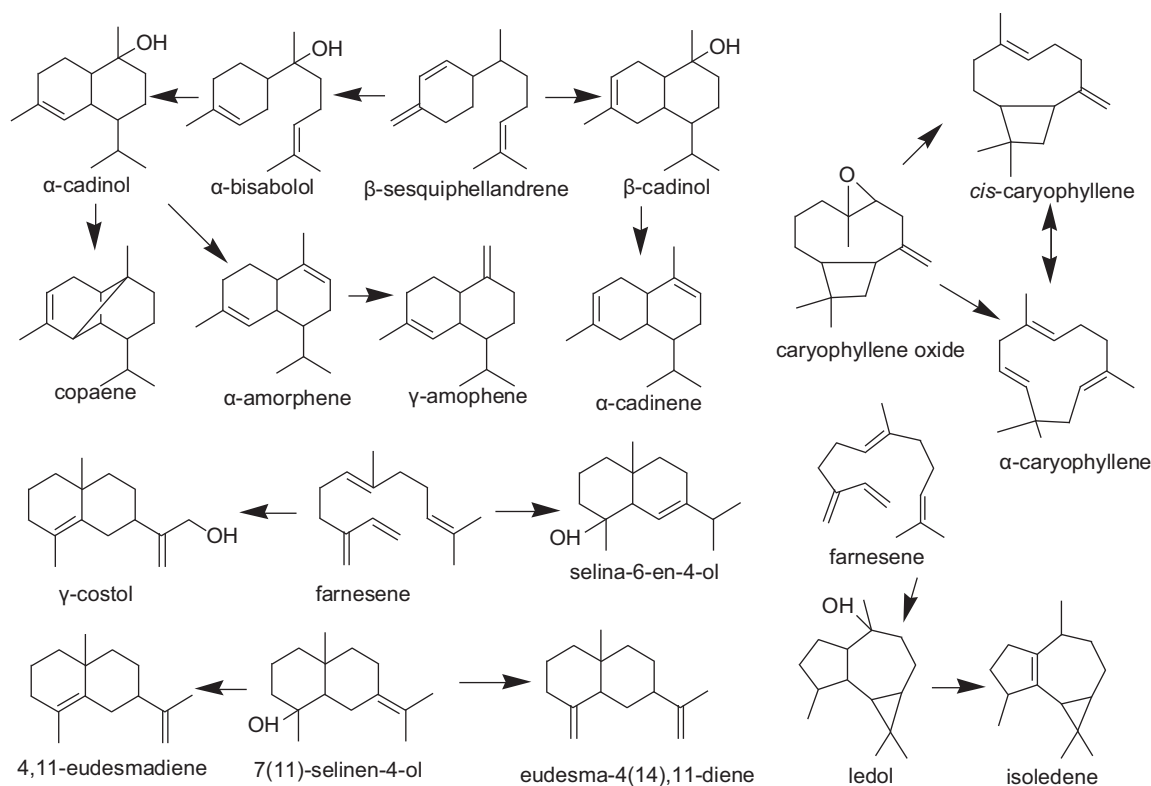


Fig. 6. The possible transformation of sesquiterpene in SF-Chrysanthemi Flos.

generate unpleasing taste. The regulation of SO_2 residues in the TCM materials is the main topic in several countries. The amount of SO_2 increased with the prolonged fumigation time; however, the amount of SO_2 can decrease if the processed medicine can be laid out for a long time. Although some SO_2 evaporates during boiling, a certain amount of SO_2 can still be involved in the reaction with some compounds to alter the quality and curative effect of TCMs. Second, detrimental heavy metals are the other significant exogenous materials. Sulfur contains several types of detrimental heavy metals, such as cadmium, arsenic, others. Inferior sulfur is often used in the manufacturing companies in China. In addition, SF results significant differences in the elements, such as sulfur and copper. For example, copper decreased in SF-*C. flos* (ju hua), which damages the quality of *C. flos* (ju hua) (Ma et al. 2011a,b). By contrast, sulfur and aluminum significantly increased in SF-*L. japonicae flos* (jin yin hua) with the increase in chromium residues (Liu et al. 2012). Third, detrimental dust produced during combustion may be deposited on the surface of the herbs. Considering the side effect of these exogenous materials, they should be strictly regulated.

Pharmacology and pharmacokinetic effect caused by SF

The pharmacology in SF-TCMs determines whether SF-TCMs can retain the desirable effect and whether the additional compounds have toxicities. Given that SF can influence the bioactive compounds of TCM herbs (as Table 1 shown), the pharmacological activity and clinical efficacy of TCMs could be reasonably affected. The compounds listed in Table 1 all have the high bioactivities in pharmacological experiments and clinic usage. Consequently, alternation of these compounds in SF-TCMs could change the herbs' original clinical effects. However, the pharmacological experiments in SF-TCMs are extremely limited. According to several reports, the abirritation produced by SF-*A. dahuricae radix* (bai zhi) weakened in the pharmacological experiments, indicating that SF affects the quality of the medicine and its curative effect clinically. In addition, the analgesic effect of SF-*A. dahuricae radix* (bai zhi) decreased drastically compared with the sun-dried variety (Ma et al. 2006). Pharmacological experiments showed that SF-*D. rhizoma* (shan yao) disturbs the oxidative stress system in the liver and the process of $\text{Na}^+\text{K}^+-\text{ATPase}$ (Guo et al. 2010). However, toxicity in the SF-TCMs has not been reported yet. No serious reports on SF-TCMs have been published. The new compound, paeoniflorin sulfonate, produced by SF-*P. radix Alba* (bai shao), showed no toxicity in animal experiments (Huang et al. 2012). Therefore, SF-TCM is a relatively safe medicine although their quality can be lowered.

SF influences the pharmacokinetic effect of TCMs. The C_{max} and AUC of sodium paeoniflorin sulfonate and benzoylpaeoniflorin sulfonate produced by SF-*P. radix Alba* (bai shao) increased, and T_{max} , as well as $t_{1/2}$, was prolonged compared with that of paeoniflorin. This condition indicated that sulfonation of the monoterpene components can improve the bioavailability and delay their absorption in mice. The structure of the new components contributes to these results (Cheng et al. 2010a), indicating that the pharmacokinetic effect of SF-TCMs can be changed because of the alteration in the compounds.

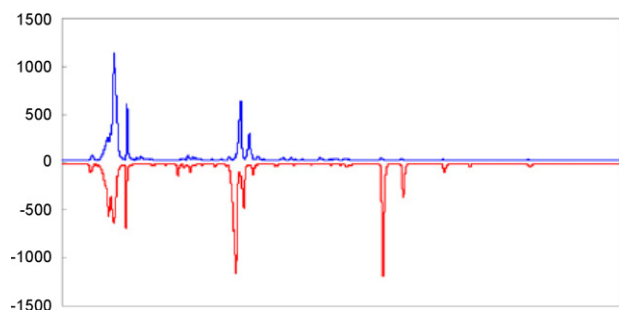


Fig. 7. Comparison between chromatograms of sulfur fumigated (upper) and sun-dried (lower) *Fritillariae thunbergii bulbus* (zhe bei mu).

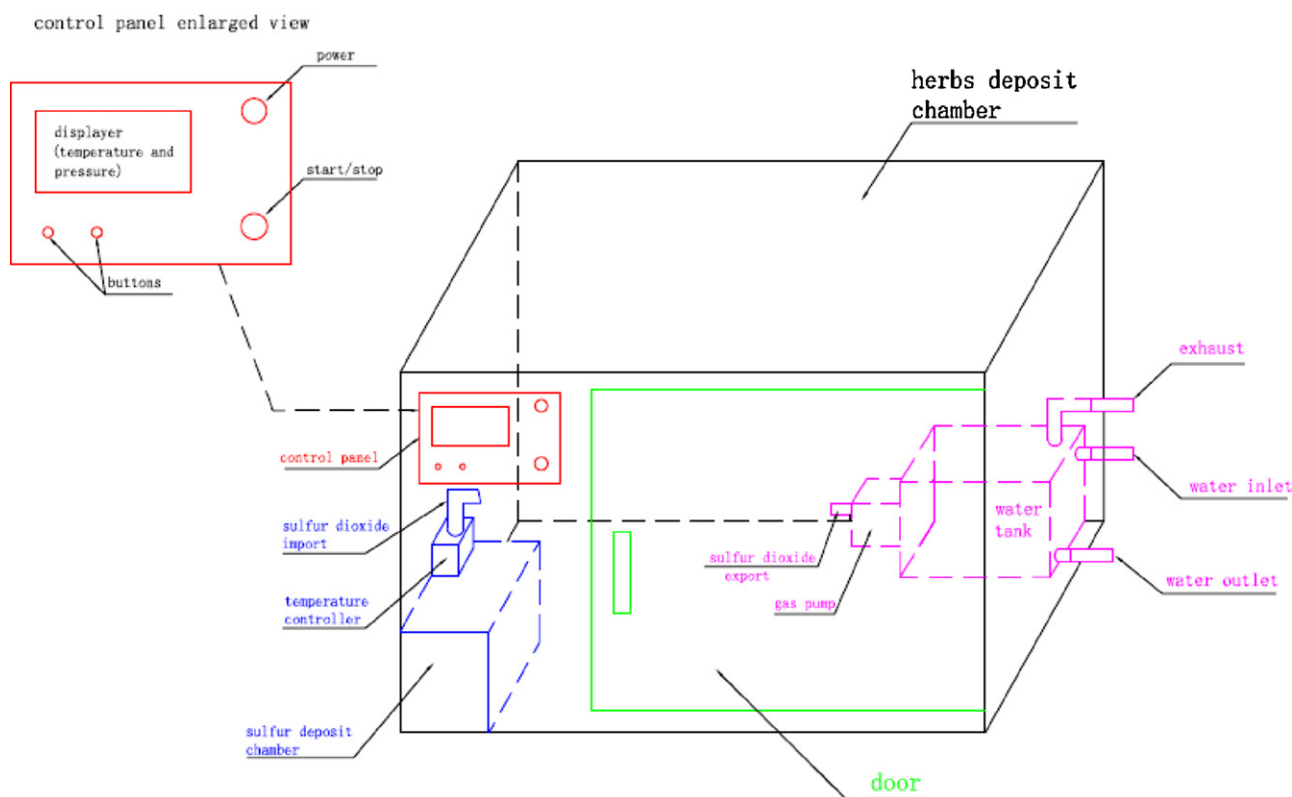


Fig. 8. The diagram of quantification-operation sulfur fumigation device (QOSFD).

Comparison between SF and other alternatives

SF is a highly efficient and relatively safe method in TCM preservation. Given the characteristics of the TCM industry, SF should focus on the following aspects: (1) The method should have long-term, not only short-term effects; (2) The materials used in this method should not react with several compounds nor damage the contents of the compounds in TCMs; (3) The method should be moisture-proof as well as anti-insect and anti-fungal effects; and (4) The optimized method preserves the color and flavor of the herbs as well as inexpensive. Natural drying and other traditional preservations are ineffective in long-term preservation. Modern technologies, including infrared radiation, microwave, and vacuum freeze drying techniques are usually expensive. These methods can only be applied in developed countries, such that their application in developing countries is impossible. These technologies preserve most of the bioactive compounds in TCMs, but its efficiency in preservation is not as high as that of SF. For example, irradiation is similar to an environmental preservation, but it is not a long-term preservation and is ineffective. Several TCM compounds can be affected by irradiation, resulting in the reduced quality of TCMs (Sivakumar et al. 2010). Zhang compared SF with the microwave processing of *Dendranthema morifolium flos* (chu ju). The volatile oil and chlorogenic acid in SF-*D. morifolium flos* (chu ju) were higher than those in the microwave-processed samples. This experiment concludes that the SF-*D. morifolium flos* (chu ju) is more efficient than the microwave-processed sample (Zhang et al. 2011a,b,c). The herb with sodium bisulfite reduced peoniflorin content along with the formation of peoniflorin sulfonate. The reaction of pure peoniflorin with sodium bisulfite also yielded peoniflorin sulfonate (Hayes et al. 2005). By contrast, SF is not only highly effective in preservation, but also costs less. This technique can be applied in developing countries in a large scale. Considering that any chemical method can influence the TCM compounds, a perfect preservation

is not feasible. Therefore, SF is apparently a better solution compared with other alternatives in preservation. This method can be optimized to decrease the loss of compounds and the addition of detrimental compounds in TCMs.

In developed countries, such as Japan and Korea, preservation of herbs depends on advanced storage and logistics technology, including infrared radiation, microwave, and vacuum freeze drying techniques. SF was used less because of its strict regulation on SO₂ residues. Several countries have strict limitation on SO₂ residues. In January 2009, Korea performed quantity limitation standard in TCMs, which regulated that the SO₂ residues in 267 TCMs must be below 30 µg/kg (30 ppm) (Duan et al. 2011). The regulated acceptable daily intake of SO₂ by WHO is (0–0.7) mg/kg. According to the requirement of WHO, a daily intake of 35 mg SO₂ for a 50 kg adult is allowable, implying that the regulated content of SO₂ in TCMs is safe. However, developing countries cannot afford these highly advanced technologies. Developing highly advanced technologies for all regions to preserve TCMs is reasonable. At present, the definite replacement of SF in developing countries is not feasible. Therefore, optimizing SF is the right path for the TCM research.

Optimized SF and QOSFD

Optimized SF is recommended because of the advantages and disadvantages of this process in TCM. Chou investigated the processing parameters in SF-*A. bidentata* (niu xi). These parameters influence the quality of TCMs (Chou et al. 2012). Wu determined that exhaustion is the most significant factor that decides the residues of SO₂ (Wu et al. 2004). Several researchers standardized the SF-*D. rhizoma* (shan yao) by investigating this factor. The thermal-device in SF has been developed with better manipulation and less pollution to the environment (Yuan et al. 2002; Formato et al. 2012). We have developed the QOSFD (Fig. 8) with key technologies such as controlling the SO₂ temperature, vacuum

processing of SF, quantification of sulfur, exhaustion of SO₂ in TCMs, and disposal of exhaust-SO₂. The content of O₂ and temperature of SO₂ are the main factors that could involve the reactions. With the control of these key factors, the reactions between compounds and SO₂/sulfurous acid can be inhibited. The quantification of sulfur in SF can guarantee the efficiency of SF with the least amount of sulfur. Controlling the exhaustion of SO₂ in SF can reduce the residues of SO₂ in the TCMs. The disposal of exhaust-SO₂ eliminates the pollutants. Through the SF device, a desirable preservation can be maintained, including torrefaction, sterilization, mildew proofing, insect prevention, and bleaching. Simultaneously, most of the bioactive compounds in the herbs cannot be damaged by SO₂ and sulfurous acid.

QOSFD mainly comprise herb deposits, sulfur deposit, temperature controller, gas pump, water tank, and control panel. Sulfur can be laid down in the sulfur deposit, where sulfur is ignited through electricity. A temperature controller was used to control the SO₂ temperature generated from the ignition of sulfur. The gas pump was used to adjust the pressure of the whole inner space, especially for the adjustment of vacuum at the beginning. The water tank should be filled with water before running, and it works for the treatment of the exhaust. During operation, adjusting the pressure to vacuum using a gas pump is the first step when the herbs and sulfur are deposited at the right places (the amount of sulfur is dependent on the amount and species of herbs). Sulfur should then be ignited in the sulfur deposit. The cooling part in the temperature controller was used to control the SO₂ temperature. After passing the temperature controller, the cooled SO₂ is discharged into the main herb deposit by the import of SO₂. The fumigation time was exactly controlled by the control panel. After fumigation, SO₂ exhaust was processed in the water tank by the gas pump and the SO₂ export. Therefore, the QOSFD is a promising optimized device for the preservation of TCM herbs.

Discussion and conclusion

Preservation is an important issue in the field of TCM. In TCM preservation, SF is the most important method with high efficiency and safety, easy operation, and low cost. However, this method influences the quality of TCMs by decreasing the bioactive compounds, producing uncertain compounds, and the SO₂ residues. In TCM preservation, highly advanced drying and preserving technologies are the best methods to control moisture and insects. However, the use of this advance technology in preserving TCMs in developing countries is not feasible at present. The field of TCMs in China should develop advanced technologies for long-term preservation. These efforts have been performed with the collaboration of colleges and corporations in China. However, in a short time run, the optimized SF has to be maintained in China in the field of TCMs. First, inhibiting the SF definitely in China caused by the insufficient the preservation technologies were impossible. Second, SF is an efficient and safe method. Third, the optimized SF, especially the development of QOSFD, guarantees the quality of the SF-TCMs. Therefore, QOSFD is significant in the field of TCMs in the recent TCM preservation.

SF indeed produces adverse effects in TCMs and these alterations lead to the weakening in pharmacology and clinic effects. These alterations in SF could not be avoided absolutely. Compared to the adverse effects caused by decaying in preservation, the risks existed in SF could be accepted. Although these alterations have not shown obvious toxicities, measurements should be performed to prevent this. Controlling the temperature and O₂ is a feasible method for preventing the alteration. To solve the SO₂ residues and heavy metals, the superior sulfur and quantification operation are necessary. However, the advanced techniques in preservation

should be developed to achieve the absolute safety in TCMs in the further.

The SO₂ regulation is reasonable for the evaluation of SF-TCMs. First, the SO₂ regulation in the SF-TCMs is necessary to ensure the quality of TCMs. Second, the SO₂ residues reflect the extent of SF in TCMs. High SO₂ residues could reflect excessive SF. The regulations in countries around the world vary. Given the huge differences in countries, requiring all countries to perform the same limitation of SO₂ is not feasible. However, in the future, the strict limitation of SO₂ in TCMs for all the countries is foreseen.

At present, SF method is controversial in the field of TCM with its high efficacy in the preservation and unconfirmed safety clinically. However, the efficiency and safety of SF are evident when compared with other methods and alternatives. QOSFD is significant and promising in the preservation of TCMs and regulation of the SO₂ residues in products. Therefore, QOSFD can be applied in the field of TCMs as well as in the other traditional medicines and herbs, agriculture, and fruit industry.

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